

REMARKS

Claims 6-12 and 14 are pending in the application. Claim 8 has been amended without prejudice and without acquiescence. Support for the amendment can be found specifically on page 4, lines 25-27. Applicants retain the right to file a continuation and/or divisional application to any canceled claims. No new matter has been added.

The outstanding issues in this application are as follows:

- Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989).
- Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469).

Applicants respectfully traverse the outstanding rejections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

I. Rejection under 35 U.S.C. 103(a) as being unpatentable over Litborn in view of Williams et al.

Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989). Applicants respectfully traverse this rejection.

First and foremost, the present references relied upon by the Examiner clearly fail to establish a *prima facia* case of obviousness. As established by *In re Royka*, *prima facie* obviousness of a claimed invention can only be established if all the claim limitations are taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). The Examiner has failed to show that all the claimed limitations are taught or suggested by the cited references.

The Examiner takes the position that Litborn (WO 98/33052) teaches a method of preventing evaporation from liquid samples in small volumes by use of a protecting liquid, typically non-miscible with the fluid containing the sample. As the Examiner has recognized, Litborn fails to teach the use of a cover liquid that is miscible with the sample liquid.

On the other hand, the Examiner asserts that one of skill in the art would combine the miscible solvent of Williams et al. to remedy the defects of Litborn. Williams et al. disclose the method of adding a miscible solvent to a capillary leading liquid sample to the *vacuum chamber* of a mass spectrometer in order to reduce the freezing point of the liquid entering the vacuum chamber via the capillary, thereby improving the reproducibility in ice formation at the capillary end. Applicant respectfully points out that Williams et al. do not teach addition of a miscible solvent to prevent *evaporation* at the capillary end, nor replacing such solvent. Additionally, Applicant points out that Williams et al. do not teach performing reactions at the end of the capillary with reactants that must be present in accurate concentrations in order to reach reproducible results. The Examiner has asserted that Williams teaches a sample loading method in which the sample is mixed with a miscible solvent for the purpose of changing a property of the sample mixture. This has nothing to do with preventing evaporation of the sample and replenishing the cover liquid preventing the evaporation of the sample, as Litborn clearly discloses.

Finally, Applicant points out that Williams et al. clearly discloses improving ice reproducibility at the end of a capillary that is *inside a vacuum chamber*. Claim 6 and Claim 8, as amended, relate to an open microarea, as opposed to inside a vacuum chamber. Williams et al. fail to disclose the open microarea of the present claims. As evaporation does not occur in a vacuum chamber, as disclosed and claimed by Williams, it would be illogical, as well as devoid of suggestion, to combine the teachings of Williams with those of Litborn.

As is well known, when an obviousness determination is based on multiple prior art references, there must be a showing of some teaching, suggestion or reason to combine the references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). In this case, there is no suggestion to combine Litborn and Williams. Applicants assert that it is implausible that one skilled in the art would have the motivation, based on any suggestion in the references themselves, to apply information leading to a more reproducible

ice formation in a mass spectrometer in a vacuum to solve an evaporation problem in an open reaction area of a microfluidic device related to keeping reactant concentrations constant. Applicants respectfully point out that the Examiner has not discussed or identified any requisite suggestion to combine the references, but merely said that one would do so. Applicants also remind the Examiner that as required by the substantial evidence rule, if the Examiner continues to maintain that Litborn and Williams et al. suggest their combination, the Examiner is requested to make of record the passage relied upon, or state for the record that no such teaching can be found in these references. *See, In re Gartside*, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir. 2000).

Thus, independent claim 8, as presently amended relates to an open microarea, further shows that there is no suggestion to combine Litborn and Williams et al. Therefore, Applicants believe that Claim 6 and Claim 8, as amended, and the claims that depend therefrom, are in condition for allowance.

II. Rejection under 35 U.S.C. 103(a) as being unpatentable over Litborn and Williams et al., and further in view of Mian (6,319,469).

Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469). Applicants respectfully traverse this rejection.

As discussed previously, Litborn does not teach the use of a cover liquid that is miscible with the sample liquid and Williams et al. do not teach addition of a miscible solvent to prevent evaporation at the capillary end, nor replacing such solvent, nor doing so in an open microarea. Therefore, Litborn in combination with Williams et al. does not render obvious claims 9 or 11, for the same reasons previously discussed. As stated by the Examiner, Mian (6,319,469) discloses a microfluidic device used to analyze microsamples, however, Mian does not teach the use of a solvent to aid in preventing evaporation, and fails to teach replenishing such a solvent. Rather, Mian discloses the use of microchannels in a disk that is rotated to utilize centripetal forces to move samples in the microchannels. The invention disclosed by Mian could not even permit replenishment of a miscible solvent for preventing evaporation, as there is no prolonged fluid connection between the pipette barrels

or hollow tubes and the inlet ports of the microfluidic device disclosed by Mian. The Examiner has failed to show, as required, that all the claimed limitations are taught or suggested by the cited references.

Furthermore, as has been previously discussed, there must be a showing of some teaching, suggestion or reason to combine the references when an obviousness determination is based on multiple prior art references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). In this case, there is no suggestion to combine Litborn and Williams, nor Litborn and Mian, nor a combination of the three. Applicants assert that it is implausible that one skilled in the art would have the motivation, based on any suggestion in the references themselves, to combine a reference that does not disclose the use of a miscible solvent with a second reference that does not disclose the use of a solvent to prevent evaporation nor replenishment of a solvent to prevent evaporation, to result in the claimed invention. Applicants respectfully point out that the Examiner has not discussed or identified any requisite suggestion to combine the references, but merely said that one would do so. Applicants remind the Examiner that as required by the substantial evidence rule, if the Examiner continues to maintain that Litborn, Williams et al., and Mian suggest their combination, the Examiner is requested to make of record the passage relied upon, or state for the record that no such teaching can be found in these references. See, *In re Gartside*, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir. 2000).

Thus, independent claim 6 and independent claim 8, as presently amended, further show that there is no suggestion to combine Litborn and Williams et al. Therefore, Applicants believe that Claims 6 and 8, and the claims that depend therefrom including 9 and 11, are in condition for allowance.

In view of the above amendment, applicant believes each of the presently pending claims in this application is in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02149US0 from which the undersigned is authorized to draw.

Dated: January 28, 2005

Respectfully submitted,

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